I. Remarks

Claims 1-6 are pending.

II. Claim rejections under 35 U.S.C. § 102(e)

Claims 1, 5, and 6 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Blaschuk *et al.*, U.S. Patent No. 6,358,920, referred to hereinafter as Blaschuk. Applicants respectfully traverse because Blaschuk does not disclose the instantly claimed adenovirus particulates.

In making the anticipation rejection, the Office has relied on two conclusions. First, the Office concludes that Blaschuk teaches that the specific polynucleotides encoding for modulation agents can be incorporated into adenoviral vectors. Next, the Office concludes that Blaschuk teaches that these adenoviral vectors may targeted for delivery using microspheres and beads. While Applicants agree with the Office's first conclusion, a close reading of Blaschuk indicates that the second conclusion is incorrect. The passage cited by the Office (Blaschuk at column 68, lines 10-37) is reproduced below:

> As noted above, polynucleotides may also function as modulating agents. In general, such polynucleotides should be formulated to permit expression of a polypeptide modulating agent following administration to a mammal. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide within a mammal, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transfected cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art. Other formulations for polynucleotides for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (i.e. an artificial membrane vesicle). The preparation and use of such systems is well known in the art. (Blaschuk at column 68, lines 10-37.)

In the above passage, Applicants respectfully assert that Blaschuk does not teach any targeting of adenoviral vectors with microspheres or beads. Rather, the Blaschuk reference teaches that there are many ways to formulate and deliver polynucleotides that "(t)hose of ordinary skill in the art will appreciate"[1] to mediate their expression in a mammal. These ways include 1) a "viral vector"[2] (such as adenovirus) comprising the polynucleotide and 2) "other formulations for polynucleotides"[3] such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems. The viral

[1] Blaschuk at column 68, lines 15-16.
[2] Blaschuk at column 68, lines 18-30.
[3] Blaschuk at column 68, lines 30-38.

vectors and the "other formulations for polynucleotides" are two separate delivery vehicles by which to achieve expression of Blaschuk's polynucleotide in a mammal. Therefore, in contrast to the Office's conclusion, the reference does not teach or suggest targeting viral particles with microspheres or beads. The viral vectors and the microspheres or beads are two independent formulation types, not components to be combined, according to Blaschuk. In fact, the only viral targeting examples present in the passage cited by the Office teach the incorporation of genes encoding for targeting moieties into a viral vector or the use of antibodies with a viral vector (column 68, 23-30.) Therefore, while Blaschuk does teach that viral vectors may be targeted, the reference is silent with respect to using microspheres or beads as targeting agent for viral vectors.

Moreover, Applicants assert Blaschuk teaches away from the instant invention. The Blaschuk reference discloses the individual components of the instant invention by mentioning adenoviral vectors and an example of a type of insoluble platform. However, as noted above, the Blaschuk reference teaches these components as two independent formulation types, not components to be combined to form a plurality of adenoviral particles complexed to an insoluble microplatform as invented by Applicants.

Therefore, Blaschuk does not teach or suggest that adenoviral vectors may targeted for delivery using microspheres and beads. The reference thus does not teach or suggest a plurality of adenoviral particles complexed to an insoluble microplatform but actually teaches away from the instant invention. Blaschuk does not and cannot anticipate the instant claims. Applicants respectfully request withdrawal of the instant rejection.

III. Claim rejections under 35 U.S.C. § 103(a)

Claims 2-4 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Mountz *et al.* (WO 98/52615) in view of Blaschuk *et al.*, U.S. Patent No. 6,358,920 and Lisziewicz et al., U.S. Patent No. 6,420,176. Applicants respectfully traverse.

In view of the prior art cited by the Office, Claims 2-4 are not obvious. The establishment of a prima facie case of obviousness requires, in part, that all claim limitations are taught or suggested by the references (MPEP 2143.03). Blaschuk fails to provide the limitation required by the instant invention of an adenovirus particulate comprising a plurality of adenoviral particles complexed to an insoluble microplatform. Therefore, no prima facie case of obviousness has been established or can be established based on a combination of the prior art cited by the Office.

As established above, Blaschuk does not teach or a plurality of adenoviral particles complexed to an insoluble microplatform. Rather, the Blaschuk reference teaches two of the many ways to formulate

and deliver polynucleotides to mediate their expression in a mammal. The ways taught are 1) a viral vectors comprising the polynucleotide and 2) other formulations for polynucleotide delivery such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems. The viral vectors and the microspheres or beads are two independent formulation types with which to deliver Blaschuk's polynucleotides for expression in a mammal. Moreover, the reference actually teaches away from the instant invention by teaching that viral vectors and the "other formulations for polynucleotides" are two separate delivery formulations.

Since the prior art cited by the Office fails to provide all the claim limitations of the instant invention, no *prima facie* case of obviousness has been established or can be established based on their combination. Applicant respectfully requests withdrawal of this rejection.

IV. Conclusion

No fee is deemed necessary in connection with the filing of this communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1074.

Respectfully submitted,

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